INCIDENCE OF ABNORMAL GTT DURING PREGNANCY POST PARTUM AND ITS CORELATION WITH PREGNANCY OUTCOME

THESIS

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USHA RAWAT

D E D I C A T E D

T O

T H E

'T R I N I T Y'

MATRE DEVO BHAVAH

PITRE DEVO BHAVAH

GURU DEVO BHAVAH

DEPARTMENT OF OBSTETRICS &
GYNAECOLOGY,
M.L.B. MEDICAL COLLEGE,
JHANSI.

C E R T I F I C A T E

This is to certify that the work entitled "INCIDENCE OF ABNORMAL GLUCOSE TOLERANCE TEST DURING PREGNANCY, POST PARTUM AND ITS CORRELATION WITH PREGNANCY OUTCOME", which is being submitted as a thesis for M.S.(Obstetrics & Gynaecology) is the original work carried out by Dr. Usha Rawat under my supervision and guidance in the department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi.

She has put in the necessary stay in the department as per university regulations.

Date : 30.11.95

(Mridula Kapoor)
M.S.,
Associate Professor & Head,
Department of Obstetrics &
Gynaecology,
M.L.B. Medical College,
JHANSI.

(CO-GUIDE)

DEPARTMENT OF OBSTETRICS &
GYNAECOLOGY,
M.L.B. MEDICAL COLLEGE,
JHANSI.

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Date : 30.11.93.

Sanjaya Sharma.

(Sanjaya Sharma)
M.D.,
Assistant Professor,
Department of Obstetrics & Gynaecology,
M.L.B. Medical College,
JHANSI.

(GUIDE)

DEPARTMENT OF PAEDIATRICS,
M.L.B. MEDICAL COLLEGE,
JHANSI.

C E R T I F I C A T E

This is to certify that the work entitled "INCIDENCE OF ABNORMAL GLUCOSE TOLERANCE TEST DURING PREGNANCY, POST PARTUM AND ITS CORRELATION WITH PREGNANCY OUTCOME", which is being submitted as a thesis for M.S. (Obstetrics & Gynaecology) was conducted by Dr. Usha Rawat under my supervision and guidance. The observations recorded have been periodically checked and verified by me.

Date : 30.11.95.

(Anil Kaushik)
M.D.,
Assistant Professor,
Department of Pediatrics,
M.L.B. Medical College,
JHANSI.

(CO-GUIDE)

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Usha Rawat

(USHA RAWAT)

CONTENT

I N T R O D U C T I O N

INTRODUCTION

Pregnancy is a diabetogenic state characterised by decreased sensitivity to insulin at cellular level. It is due to hormonal changes occurring in pregnancy (Fineberg et al, 1987).

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance with onset or recognition first during pregnancy.

Diagnosis is based on an abnormal glucose tolerance test as defined by O'Sullivan and Mahan(1964).

It is important to identify a pregnant woman with gestational diabetes mellitus, because GDM is common and associated with significant metabolic alteration, increased perinatal mortality and morbidity and maternal morbidity and subsequent development of diabetes in mothers in a large proportion of cases.

Perinatal mortality significantly increases in gestational diabetic pregnancy if the metabolic alteration is not recognised or if it is recognised but not treated properly. In addition to increased risk of intrauterine foetal deaths. Commonly reported perinatal morbidity associated with GDM included an increased incidence of macrosomia, birth trauma, neonatal hypoglycemia, hyperbilirubinemia, hypocalcemia, RDS and polycythemia.

Gestational diabetes mellitus has a short term and long term maternal morbidity. Short term maternal morbidity includes an increased incidence of hypertension, hydroamnios and caesarean section, and long term maternal morbidity includes increased likelihood of carbohydrate intolerance after delivery. A significantly increased risk of (type II DM) non insulin dependent diabetes later in life and predisposition to obesity, hyperlipidemia, atherosclerotic vascular diseases and increased blood pressure and mortality.

The offsprings of woman with GDM have a higher incidence of childhood obesity, type II DM, during childhood, and later in life and intellectual and behaviour impairment (Pettitt et al, 1985).

The purpose of the screening is the early detection and treatment of a disorder that carries a adverse prognosis with no symptoms(Fletcher and Spitzer, 1980).

Screening can be justified only if there is a scientific evidence that the outcome of the disorder is better when treatment started before, rather than after the appearance of symptoms. Gestational diabetes satisfy both these criteria. The hyperglycemia associated with neonatal hazards is asymptomatic for the mother, gestational glucose intolerance identifies woman at risk of subsequent diabetes mellitus (Mestman et al, 1972 and O'Sullivan and Mahan, 1980).

American Diabetes Assoation (1987) had recommended that all pregnant women should be screened at 24-28 weeks of gestation. Screening should be performed when the anti-insulin effects of the pregnancy is optimum. Toranovic and Peterson (1985) recommended that all pregnant women should be screened between 27-31 weeks of gestation to obtain the highest yield. It has recommended based on both cross sectional and longitudinal studies (Merkatz et al, 1980).

Though lots of work had been done from time to time over pregnant diabetic mother and their infants very little data are available on gestational diabetes and impaired gestational glucose tolerance while only Tellerigo et al (1980) had worked over pregnant mothers with two hour plasma glucose levels between 120-164 mg/dl , the levels which considered to be within normal range and they found that these mothers had increased incidence of macrosomic babies.

This study was planned to further study the effects of abnormal gestational glucose tolerance over mothers and newborn, so that timely treatment can be given to the expecting mothers and neonatal morbidity and mortality can be reduced.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The syndrome of diabetes mellitus (DM) is characterised by disorder of metabolism of carbohydrate, protein and lipid due to insulin deficiency and or insulin resistance evolving from interaction of variety of genetic and environmental factors. Metabolic derangement manifest by chronic hyperglycemia with or without hyper lipidemia and a tendency to develop to ketoacidosis.

Charakaa and Sushruta (600-400 BC) of ancient India recognised many of the currently known facts of the disease and named it MADHUMEHA (Rain of honey) having noted sweetness of urine.

The name diabetes was coined by Areteus in the century AD. Claud Bernard (1850) was the first to note hyperglycemia as a cardinal feature of diabetes.

Gestational diabetes is defined as "Carbohydrate intolerance of variable severity with onset or first recognition during pregnancy (American Diabetes Association, 1986). Condition is associated with increased perinatal mortality, even when diagnosis is made (Donald R Caustan).

Gestational diabetes mellitus is defined as glucose intolerance first recognised in pregnancy(Metzgr, 1991), this definition includes mothers with previously undiagnosed diabetes or impaired glucose tolerance whose glucose intolerance is first recognised in pregnancy.

Gestational DM usually develops in the 2nd trimester induced by maternal changes in CHO metabolism and insulin sensitivity (Kuhl, 1991).

The diagnosis of GDM has implication affecting both the pregnancies and the future health of the mother.

A GDM pregnancy may also have a detrimental effect on the future health of the child.

INCIDENCE AND PREVALENCE OF GDM

The prevalence of GDM is highly dependent on the ethinicity (Hadden, 1985, Beischer et al, 1991).

Compared with white of European women, the prevalence rate for GDM is increased approximately eleven fold in women from the Indian subcontinent, eight fold in south east Asian women and six and three fold in the Arab/Mediterranean and black/Africo-caribbean women respectively (Dornhurst et al, 1992).

There are geographical differences in the prevalence rate for GDM in the U.K. due to ethnic difference in the local population with prevalence rate of ranging from 1-5% from an inner London Antenatal Clinic (where 34% of mothers ethnic minority group, Maresh and Beard, 1989) to 0.2% in Belfast with a predominantly white/European population (Hadden, 1980).

Increasing maternal obesity, age and family history of diabetes are additional important independent risk factors for GDM (O'Sullivan et al, 1973; Maresh and Beard, 1989 and Roseman et al, 1991).

Age also is an important factor. Mestman (1980) reported that the incidence of gestational DM was 3.7% in women younger than 20 years, 7.5% for those 20-30 years and 13.8% for women older than 30 years.

Overall incidence of GDM is approximately 2% (O'Sullivan et al, 1964).

The incidence of gestational diabetes lies between 1-5% (Stephen et al, 1981).

In a Malaysian Hospital population the incidence was around 1.3% (Being 62.5% Malayas, 20.3% Chinese, 12.9% Indian and 4.8% others) (Nik, 1988).

The incidence of the GDM has been estimated between 3 and 15% percent depending on the population studied and the diagnostic criteria used (Gabbe, 1985).

PREGNANCY OUTCOME IN GESTATIONAL DIABETES

Pregnancy outcome in mothers with established diabetes is highly dependent on maternal glycemic control. throughout the pregnancy(Karlsson and Kjellmer, 1972).

The pregnancy related morbidity and mortality in GDM is less than that for established diabetic women, however, if left untreated it is significantly higher than for non diabetic women(Beischer, 1975; Abell and O'Sullivan et al, 1979b and Petit et al, 1980).

Maternal obesity is a frequent and important co-existing risk factor in GDM and is an independent contributor to the increase in perinatal morbidity

associated with fetal macrosomia(Maresh et al, 1989; Green et al, 1991) but not for the neonatal hypoglycemia, polycythemia, hyperbilirubinemia, hypocalcaemia which are related to the degree of the neonatal hyperglycemia (Maresh et al, 1989 and Hod et al, 1991).

Unlike established diabetes there is no increase in the congenital malformation rates as significant maternal hyperglycemia in GDM occurs after organogenesis is complete (Petit et al, 1980).

PHYSIOLOGY OF GESTATIONAL DIABETES MELLITUS

Diabetes mellitus, a metabolic syndrome of diverse etiologies is characterised by abnormalities of glucose, fat and protein metabolism.

These derangements in fuel metabolism results from inadequate insulin replacement. This state of relative and/or absolute insulin deficiency results in fasting and postprandial hyper-aninoacedemia and hyperlipidemia as well as hyperglycemia.

These effects are further escalated in pregnancy by the insulin antagonistic hormones which are secreted by the placenta.

The excessive delay of the substrates to the fetus and the resulting fetal hyperinsulinemia are believed to contribute to the adverse pregnancy outcome associated with poorly controlled diabetic mothers.

Many investigators have demonstrated that insulin resistance occurs in pregnancy(Fischer et al, 1974; Lind et al, 1979 and Morliss, 1979). Rising levels of maternal plasma progesterone, human placental lactogen, free cortisol and prolactin have been implicated in this process. Human placental lactogen levels rise steadily during the 1st and 2nd trimester and the reach a plateau in the last 4 weeks of pregnancy. The diabetogenic effects of the HPL results in the mobilization of lipids as free fatty acids. These free fatty acids serve as a maternal energy source thereby making glucose and aminoacids available to the fetus.

Cortisol levels also rise during pregnancy. Cortisol stimulates endogenous glucose production and glycogen storage and decreases glucose utilization thereby reducing the effectiveness of insulin.

Prolactin which is increase 5 to 10 folds during late pregnancy has a significant influence on pancreatic islet cell insulin secretion especially during late gestation.

NORMAL PREGNANCY : FASTING STAGE

Glucose Metabolism

During normal pregnancy the fasting blood glucose levels decreases. Lind and Aspilloga (1988) have demonstrated that fasting glucose concentration reach their nadir at both the 12th week of gestation and remain at this level until delivery. Felig and Lynch (1970) have also reported

decrease of 15 mg/dl in glucose levels of pregnant women after an overnight fast.

At the same time fasting insulin level increase from 5 micro unit/l to 8 micro unit/l at term, however, little change is seen in the first and second trimester when the glucose values reach their nadir. This provides a cause and effect relationship between fasting glucose and insulin levels.

Kuhl and Holst (1976) have also demonstrated that the insulin/glycogen ratio in pregnancy increases significantly when compared with that in the nonpregnant state.

Fat Metabolism

Accelerated fat metabolism and ketone body formation of well documented in pregnancy particularly after long period of steroids. Two phases of adipose tissue metabolism have been proposed by Knopp and colleagues (1973). As initial increase in fat storage during mid gestation and diminished fat storage mobilization is enhanced. All three lipoprotein fractions (LDL, HDL and VLDL) rise during normal pregnancy.

Protein Metabolism

It is generally believed that the concentration of most aminoacids are lower in maternal plasma during pregnancy than in the postpartum period.

Young (1976) reported decrease in the plasma level of total alpha amino nitrogen from 3 mM in the non pregnant state to 2-3 mM during pregnancy.

RESPONSE TO GLUCOSE LOAD

A suppression of endogenous glucose production and an acceleration of glucose utilization is normally seen after a carbohydrate containing meal. In non-pregnant women, plasma glucose levels reach their peak 30 minutes after the ingestion of a glucose load and return to baseline at approximately 1 hour but during pregnancy at term glucose level were higher and reach their peak approximately 60 minutes after the glucose ingestion. The decline to base the was slower and fasting levels do not regained for about 2 hours.

Insulin response is also altered in pregnancy. Insulin levels reach their peak at about 1 hour after ingestion of a glucose load when glucose value are also peaking insulin levels decline slowly and still are not back to base line at 2 hours. For any given glucose challange, the pregnant woman is stimulated to produce additional insulin, but her blood glucose level remain elevated for a longer period of time. This leads to the concepts of the "insulin resistance" during pregnancy which is felt to be mediated at the post receptor level (Puavilai et al,1982).

The metabolic response to feeding in pregnancy is characterised by hyper insulinemia, hyperglycemia and hypertriglyceridemia accompanied by a decrease in circulatory glucagon. These adoptation have been termed facilitated anabolism by Freinkel et al, 1974).

Catalano and colleagues (1991) assessed the longitudinal changes in insulin release and insulin sensitivity in non obese normal pregnancy during gestation. They evaluated 6 women with OGTT body composition analysis intravenous GTT and hyperinsulinemic euglycemic clamp before conception, at 12 to 14 weeks and 34 to 36 weeks gestation. They found a significantly increase in the insulin glucose ratio during the OGTT performed during pregnancy.

They also reported a significant 3 to 3.5 fold rise throughout gestation in the 1st and 2nd phase insulin release during the IGTT as well as a decrease in insulin sensitivity through 36 weeks gestation. They concluded that there is decreased peripheral insulin sensitivity in pregnancy.

Thus normal pregnancy is characterised by fasting hypoglycemia with exaggerated glucose and insulin level postprandially as compared to the nonpregnant state(Pheips PL et al). Woman who are not able to augment pancreatic secretion sufficiently to overcome pregnancy induced insulin resistance in the latter part of gestation, will develop excessive post prandial glucose concentration resulting in gestational diabetes when this insulin deficiency is severe fasting hyperglycemia also develop.

The studies of Fisher et al (1980) using a high dose glucose infusion test showed that normal pregnant women /85th percentile standard of body weight at 38 to

40 weeks of gestation had a decrease of about 80% in the insulin sensitivity index of that observed in the non pregnant group.

Buchanan et al (1990) with the minimal model technique, found that insulin sensitivity in normal pregnant women at 29 to 36 weeks gestation was only 1/3 of that of a group of normal nonpregnant women of a similar age and relative weight.

Diabetes occurs in about 1% of pregnant women of these only one in 10 will have been known to have had diabetes prior to pregnancy.

Women who are known to be diabetic prior to pregnancy have been classified by Dr. Priscilla White into categories :

Gestational DM : Abnormal GTT but euglycemic maintained by diet. Diet alone insuffice insuline required.

Class A : Diet alone any duration or age for onset.

Class B : Onset age 20 or older and duration ⟨10 years.

Class C : Onset age 10-19 years or duration 10-19 years.

Class D : Onset age ⟨10 years and duration ⟩20 years or background retinopathy or hypertension.

Class R : Proliferative retinopathy or vitreous haemorrhage.

Class F : Nephropathy withover 500 gm/day proteinuria.

Class R & F : Criteria for both class and F Co-exist.

Class H : Atherosclerotic heart disease, clinically evident.

Class T : ~~Prior~~ Prog after renal transplantation.

Glucose tolerance returns to normal in the majority of women with GDM, but a small but important proportion of women will have abnormal GTT. These include women in the process of developing IDDM and those with impaired glucose tolerance or NIDDM which predected pregnancy(Damm et al, 1984; Buschard et al, 1987 and Dornhorst et al, 1990).

IDDM is an autoimmune disease with a long subclinical prodromal to have (Gorsuch et al, 1981), which is unmasked by the metabolic changes of pregnancy (Buschard et al, 1987).

Approximately 5% of GDM women develop IDDM within 5 years of the index pregnancy(Damm et al, 1989; Dornhorst et al, 1990). Clinical features which should alert one of the possibility of IDDM include age ⟨30 years, lack of obesity and first pregnancy and no family history of DM (Dornhorst, 1990).

All women with normal glucose tolerance post partum must be considered at greatly increased risk of diabetes in future pregnancy) Philipson and Super, 1989) and non insulin dependent diabetes in later life.

Approximately half of the previous GDM women will develop impaired glucose tolerance or non insulin dependent tolerance within 10 years of their index pregnancy (O'Sullivan, 1982).

The majority of previous GDM women who gom on to develop impaired glucose tolerance after a period of

normal glucose tolerance would be expected to become diabetic during their life (Keen et al, 1982 and Yudkin et al, 1990), as determination of the glucose tolerance occur with increasing age, increasing obesity and decreasing physical activity.

Diabetes adversely affects vascular disease (Kannel and Mc Gee, 1979a) morbidity from coronary heart disease is increased four to five fold in diabetic women and is the commonest cause of death.

EFFECT OF THE DIABETES ON THE PREGNANCY

1. Spontaneous Abortion

The rate of spontaneous abortion in women with diabetes is no greater than in the general population of pregnant women without diabetes.

Recent articles suggest that those with metabolic control are at increased risk of spontaneous abortion as compared to women with good blood glucose control.

The diabetic women who aborted had significantly higher fasting and postprandial glucose level in the first trimester as compared to those who continued pregnancy to viability.

Increase in glycosylated haemoglobin level by one standard deviation carries an increase of 3.0% risk of spontaneous abortion (Mills et al, 1988).

2. U.T.I.

The mechanical changes in renal drainage brought about by the enlarging uterus cause stasis and increased risk of pyelonephritis. Asymptomatic bactriuria should be treated.

Pyelonephritis may precipitate ketoacidosis and is itself considered by Pederson (1975) to be prognostically bad sign.

U.T.I. in nondiabetic women are knwon to adversely affect perinatal mortality especially if maternal hypertension or acetonuria is present obviously. These complications may occur in the diabetic women.

3. Headache

A few women develop severe headache which required hypnotic or narcotic treatment.

4. Pre-eclampsia

Pre-eclampsia has histogically been a frequent complications of diabetic pregnancy (White et al, 1971) with poor prognosis for the fetus. The incidence of pre-eclampsia or eclampsia was significantly greater in a group of patients with one abnormal OGTT values when compared to women whose screening tests results were normal (Lindsy M.K. et al, 1989).

Tallarigo et al (1986) found that even with normal GTT results as defined by the Medical Diabetic Data

Group criteria after 2 hour plasma glucose levels were associated with a significant increase in the incidence of macrosomia and congenital abnormality as well as toxemia and caesarean section.

In a territary Malaysian hospital the maternity hospital, Kuala Lumpur (MHKL) the incidence of pregnancy induced hypertension disease is about 7-8% in patients with diabetes the incidence may be 10-20%.

Lauri Suhonen and associates (1992) reported that the frequency of both chronic hypertension and pregnancy induced hypertension and pre-eclampsia were higher in gestational diabetic group as compared with controls.

5. Polyhydroamnios

Polyhydroamnios occur in one third of our patients It is more common in the diabetic women and not related to congenital anomalies. Premature prevalence labour precipitate by the polyhydroamnios is the most serious complication (Joslin Diabetes Mellitus).

This occurs in about 20% of diabetic patients. The increase being directly influenced by the blood sugar variation.

6. Still Birth

Death of the fetus in the last weeks of pregnancy is the classic obstetrical accident in the diabetic mothers.

It is not related to the severity or duration of diabetes because it occurs also in women with gestational diabetes treated with diet alone.

7. Placenta

Placenta from diabetic mothers tend to be heavier than those from nondiabetic mothers with fetuses at the gestational age and weight.

In women with renal disease the placenta is often smaller not unlike those from women with non diabetic renal diseases.

John and Kitzmitler et al (1978) studied 147 diabetic women. Out of them 71% were dependent on insulin for 7/10 years ambutatory management of the diabetes was done with weekly clinic visit until hospitalization at 36 to 37 weeks gestation. Modern method of foetal assessment were applied and the timing and route of the delivery individualized of the patients. 35% were delivered at or beyond 38 weeks of gestation. The primary LSCS rates was 55%, polyhydroamnios was a frequent maternal complications and was associated with the premature labour and still birth in two cases. Polyhydro-amnios was least common in women with the lowest mean out patient blood glucose.

BABY

GESTATIONAL DIABETES AND PERINATAL MORTALITY

O'Sullivan et al (1973) studied all pregnant women between 1962 to 1970. They were screened with a blood glucose estimation 2 hour after a 50 gm oral glucose load. Those with a glucose value ≥130 mg% were tested with 3 hour 100 gm OGTT. Four (1.5%) of the 295 women with normal OGTT had a perinatal loss as compared to 12 (6.4%) of 187 women with an abnormal GTT.

Sutherland and Stowers (1975) reported the results of 1800 intravenous glucose tolerance test done on 1600 women during pregnancy with various indications suggestive of diabetes. It can be seen that the rate of fetal loss increases eight fold as the number of the indications for GTT is increases from 1 - 4.

Hadden (1975) has also shown that certain indications for glucose tolerance testing are associated with increased perinatal mortality rate, in particular previous perinatal loss or fetal anomaly, which carries a fetal death rate of 7% to 9.8% as compared to a rate of between 6-8 and 4-5% in the hospital population during the same time period.

Abell and Beischer (1975) reviewed 2000 consecutive women who had a 3 hour 50 gm OGTT in the third trimester of pregnancy. An abnormal test was associated with a perinatal mortality of 31.7% per 1000 as compared to 9.8 per 1000 if the glucose tolerance test was negative.

Pedersen proposed that maternal hyperglycemia causes fetal hyperglycemia and hyperinsulinemia with a consequent increase in fetal growth. Although the cause of the late intrauterine death remain uncertain. It may be the result of the fetal hyperinsulinemia causing an increased metabolic rate and tissue hypoxia.

Petit et al (1980) reported an 75 gm 2 hour OGTT done in the early third trimester of 811 pregnancies among Pima Indian women. The PNMR was directly proportional to the 2 hours plasma glucose levels, with ⁄120 mg% associated with 5/1000 and values between 150-199 of associated with the rate 44/1000.

CONGENITAL MALFORMATION

The incidence of the congenital malformation in the offsprings of the diabetic mothers is estimated 6-13% as compared with 1-3% of normal population. Moshe Hod et al reported the incidence of minor congenital anomalies between 19.4-20.5% and major congenital malformation 1.8 - 6.82%.

Almost all investigators found an increased incidence of major both dependent in offsprings of the diabetic mothers as compared to those of control group. Studies of the incidence and pathogenesis of the congenital anomalies in the IDM have been reviewed by Gabbe et al(1977).

Varied type of the anomalies including enencephaly, meningocoele trsnsposition of the great vessels of

the VSD, coarctation of the aorta, caudal regression syndrome and vertebral dysplasia, ureteral duplication, renal agenesis and atresia are observed in a retrospective view.

The occurrence of the anomalies is more likely to be related to metabolic mileau in the early pregnancy than to genetic determinants. The crucial period of the teratogenesis for the common anomalies in infants of the diabetic mothers occur within 9 weeks of the last menstrual period (i.e. within 7 weeks following conception (Joslin's Diabetes Mellitus). Foe this reason good control of the diabetes mellitus is in the earliest possible weeks of gestation.

More recent evidences indicate that ketone bodies in combination with glucose are responsible for teratogenic effects.

Naeve (1967) found no rise in malformation in infants born to diabetic father and non diabetic mothers as compared to the normal father.

Pedersen Coller and Naeve et al reported an increase risk of congenital anomalies in infant born to mother with white classes D, F and R diabetes suggesting associations with maternal disease and vascular complications.

There are multiple etiologie factors in the increased incidence of anomalies in IDDM. The role of the genetic factors has not been substantiated.

Molsted Pederson and associates (1964) speculated that fetal hypoxia could play a role in diabetic preg-

complicated by vascular diseases but they later in 1977 concluded that better metabolic control in the same group of patients reduced the risk of the birth defects.

Hamrak (1971), Ingalls et al (1956) and Landauen (1947) studied that hypoglycemia may be associated with an increased risk of the fetal malformation. Insulin injected into chick and rodent embryos produced vertebral and bony anomalies. The anomalies were reduced when hypoglycemia was prevented by adding glucose to the preparations.

Horii (1966) found that hyperglycemia may also be a cause of fetal anomalies litters born to the diabetic mice have an increased incidence of limb malformation and Cleft palate. When the mothers are treated with insulin this increased incidence is eliminated. While the mechanism of the effect of hyperglycemia is uncertain it may involve the role of the collagen in inducing the embryogenesis.

Fibroblast grown in a medium containing a high level of glucose secrete more collagen as compared with fibroblast in a medium containing physiologic amounts of glucose. A large amount of this collagen may be converted to glycosyl and one can speculate that alteration of the collagen molecule in terms of CHO may affect the induction process since fetal hyperglycemia in the IDM should until the fetal pancreas is functional well after the major period of the morphogenesis endogenous insulin should not be a cause of malformation (Villee et al, 1977).

Pedersen commented that 40% perinatal mortality results from congenital malformation. Same observation was done by Gabbe et al (1977). Joslin's Clinic has also observed a subtantial incidence of congenital anomalies 9% major and 5% minor. Among the congenital malformations highest percentage is of neural tube defects and cardiac anomalies.

Freinkel (1980) referred to pregnancy on a tissue culture experience where the maternal insulin determines to a large extent the culture medium. Any medium alterations significantly influences embryo and fetal development.

MACROSOMIA

Complications from diabetes in late pregnancy augmented fuel delivery to the fetus results in hyperglycemia. B cell activity enhances infant growth in diabetic mothers with minimal hyperglycemia,

The adverse outcome most frequently associated with gestational diabetes is fetal macrosomia upto 30% of infants of mothers with an abnormal GTT have a birth weight of more than 4000 gm (Philipson et al, 1985; Gabbe et al, 1977 and Cousten and Lewis, 1978).

However, Spellacy et al (1985) found that only 29 of 574 (5.1%) infants with a birth weight more than 4500 gm were born to women with gestational diabetes.

As the background incidence of infants more than 4500 gm was 1.7%, the relative risk of macrosomia with

gestational diabetes was 3.0. By comparison 44% of the macrosomic infants born to mothers weighing more than 90 kg (relative risk - 25.8) and 10.4% to women beyond the 42 weeks of gestation (relative risk - 6.4). This report suggests that heavy mothers and post term pregnancy are much more closely associated with fetal macrosomia as compared to the gestational diabetes mellitus.

Oat et al (1980) reviewed the results of a 50 gm 3 hour OGTT performed in 137 women who delivered an infant weighing more than 4540 gm only 32(23%) had an abnormal GTT.

Moshe Hod et al reported the incidence of macrosomia 5.6 - 20% in diabetic mothers.

In one study Tellarigo et al (1986) showed that even limited degree of the maternal hyperglycemia which are currently considered to be within normal range i.e. two hour plasma glucose levels between 120 to 164 may affect the outcome of the pregnancy in the form of macrosomic baby.

Postulated mechanism of macrosomia is that maternal hyperglycemia results in fetal hyperglycemia an excessive stimulants of the fetal pancreas to produce insulin. There is strong correlation of glucose level in maternal and fetal blood stream. Insulin facilitates the transportation of nutrients like glucose aminoacids and free fatty acids into cells (Pedersen et al, 1977).

Another possible mechanism is the transplacental passage of aminoacids released from the maternal proteins which stimulate the fetal islet cells.

It is widely accepted that fetal growth is a complex multifactorial process. However, in the pregnant diabetic fetal growth complications are considered to be the consequence of hyperglycemia, which is one of the cornerstone of the diabetic fetopathy. In fetal life insulin is the most recognised regulatory hormones for fetal growth. Although presents at 8-10 weeks of gestation insulin remains relatively inactive until 20 weeks of gestation (Adam and associates, 1969).

Additionally the number of the insulin receptors in the human fetal liver becomes maximal at 19 to 25th weeks. Furthermore there is increased affinity of insulin in late gestation (Neufeld et al, 1980).

The major effect of insulin on delate and acdentuated fetal growth and fat deposition occur late in gestation (Gluckman et al, 1986).

Studies indicated that glucose is a less efficient stimulus to insulin release in the fetus than in adults. However, a sustained increase in fetal blood glucose in the presence of arginine or leucin can markedly enhance the fetal insulin release. Since muscle tissue is quite sensitive to insulin, this offers a possible explanation for the fact that women with mild diabetes and modest hyperglycemia sometimes deliver macrosomic infants.

Shima and associates found a strong correlation between birth weight of overgrown infants aud the infants serum insulin levels.

The main clinical implication of fetal macrosomia is birth injury and shoulder dystocia.

Ganne et al (1977) noted that 10% (5/49) of infants weighing more than 4000 gm suffered seriously birth trauma (fractured bone or peripheral nerve injury) as compared to 2% of normal sized infants born to mother with gestational diabetes mellitus.

David et al reported that the incidence of birth weight of 4540 gm or more rose from 0.87% in the year 1971 to 1977 to 1.16% in the 12 years from 1978 to 1989 with a concomitant increase in hyperglycemia in over antenatal population.

The results from glucose tolerance tests performed routinely during the pregnancies of 510 women who delivered a infants with a birth weight of 4540 gm or more were compared with those from a control series of 5603 women with consecutively tested pregnancies, glucose tolerance in the subsequent pregnant women also compared with the control series and in 1991 the study group were investigated for emergence of permanent diabetes mellitus. Excessive birth weight was associated with maternal hyperglycemia but not with gestational diabetes. 79% of the infants with birth weight more than 4540 gm were born to mothers who were not hyperglycemic. There was no increase in glucose tolerance in subsequent pregnancies in the study group. Only 2 of the 49 women with follow up testing had diabetes mellitus. Birth weight more than 4540 gm occurred in 1.1% of the total

population and 1.17% of women with gestational diabetes and was related with maternal hyperglycemia 1 in 5 cases.

HYPOGLYCEMIA

A common problem in infants of diabetic mothers is early postnatal hypoglycemia, secondary to excessive insulin secretion after the division of the umbilical cord and the termination of placental transfer of glucose. However, the association of severe neonatal hypoglycemia with cord insulin levels has not been demonstrated in all studies.

Neonatal hypoglycemia appears to be most uncommon even in macrosomic infants. Philipson et al (1985) found only 4 infants with hypoglycemia out of 158 pregnancies with abnormal GTT.

Although Gabbe et al (1977) reported a 7% incidence of hypoglycemia in the infants of 261 class A diabetes, approximately 25% of these women were delivered before 38 weeks of gestation.

Jonson and Bloom suggested that the neonatal pancreatic glucagon response to the post natal fall in glucose is inappropriately small in the infant diabetic mothers, specially in cases with sustained hyperglycemia.

Studies by Kuhl et al (1981) and Midovinik et al (1987) have shown that high maternal blood glucose concentration at delivery increases the risk of neonatal hypoglycemia.

E. Stenningr et al (1991) in their study observed 38% incidence of neonatal hypoglycemia in infants of mothers with insulin treated gestational diabetes mellitus. Hypoglycemia occurs most frequently 2 hour after birth. Neonatal hypoglycemia leads to neural dysfunction. Aynstey Green et al (1987) reported acute cerebral dysfunction in newborns with blood glucose concentration less than 2.6 m mol/l.

NEONATAL PULMONARY COMPLICATIONS

RDS is the neonatal manifestation of insufficient fetal pulmonary synthesis storage and release of surface active phospholipid.

Hubbel and associates (1959-1964) found an overall incidence of RDS of 27% in a study of 473 live births IDDM to the Boston hospital for women from 1959 to 1964. In these studies prematurity and caesarean section were thought to be the major causes of RDS.

Robert and associates retrospectively studied 805 live birth IDDM birth at BHW from 1958 to 1968 and found an incidence of RDS of 23% as compared to an incidence of 1.3% in infants born tc nondiabetic mothers.

Maternal diabetes state affects fetal lung development. The exact mechanism of this interaction has been examined in a cell culture system by Smith and associates (1975). They utilised a monolayer cell culture system of the fetal rabbit lung and examine the effect on lecithin synthesis when insulin was added to the culture system. They found that although insulin alone results in a small

but significant increase in lecithin synthesis. The addition of insulin and cortisol to cell culture results in a marked diminution. The stimulation effect observed when the cortisol alone was added. Since cortisol is thought to be the physiologic stimulus for the increased synthesis of lecithin in the fetal lung seen at approximately 90% of the term gestation. They hypothesized that insulin might interfere with this normal increase in lecithin synthesis. The increase in the lecithin synthesis is responsible for the normal functioning of the neonatal lung at term. Therefore, the elevated insulin concentration in plasma in IDDM may interfere with this normal maternal sequences and lead to the increased incidence of RDS in the IDMs.

NEONATAL HYPERBILIRUBINEMIA AND HYPOCALCEMIA

Hyperbilirubinemia and hypocalcemia are commonly found in the early life of the IDM. Hyperbilirubinemia was noted in 38% of the newborn infant studied by Pedersen(1977) and 27% of those studied by Essex and co-workers (1973). These authors used a 10 mg/dl bilirubin level the cause of the hyperbilirubinemia is presumed to be related to the functional prematurity of hepatic enzyme necessary for the conjugation of the bilirubin (Osler and co-workers, 1983).

Tsang and colleagues (1972) demonstrated hypocalcemia in 6 of 10 infants of mothers with white classes for B,C and D. The incidence of hypocalcemia was increased over that in a matched control group even when gestational age

and perinatal complications were considered.

Pedersen (1977) found hypocalcemia in 10% IDDM in a recent series. The cause of the hypocalcemia was not known.

POLYCYTHEMIA

Prevalence of the polycythemia was reported as 3.8-13.3% in infants of gestational diabetes by Moshe et al (1991).

Similar observations were done by Ranade et al (1989). In their study they reported the prevalence of polycythemia in 10% IGDM.

According to Pedersen hypothesis maternal hyperglycemia lead to fetal hyperinsulinemia, which in turn suppresses the synthesis storage and release of surfactant, leading to HMD. These pulmonary complications of the diabetes leads to fetal hypoxemia. This hypoxemia stimulates haemopoietic system leading to polycythemia.

PREMATURITY

Ranade et al (1987) in their study reported prematurity in 28% of GDM. Deodari et al in their study showed that 20% of infants born to gestational diabetes were premature.

RISK FACTORS FOR GESTATIONAL DIABETES

Miller and associates (1944) reported the quantitative relationship between histories and excessive fetal

hypoglycemic agents must not be used in antenatal period as these drugs cross the placental barriers leading to neonatal hypoglycemia.

Dietary Therapy for Gestational Diabetes

The goal of dietary therapy include the avoidance of large amounts of concentrated and refined sugars which may cause rapid perturbation in circulatory glucose levels and the maintenance of consistency from day to day to allow accurate assessment of metabolic control. Adequate caloric intake is required for nourishment of developing fetus, however, excessive consumption may lead to excess weight gain exercerbating insulin resistance and rising circulatory glucose levels.

Gabbe et al recommended caloric requirements for gestational diabetics of 200-220 calories daily meal plan include 3 meals and a bed time snack.

If dietary therapy does not achieve adequate glycemic control, insulin therapy should be instituted .

Insulin Therapy

If insulin is used highly purified porcaine insulin or human insulin sould be administered to decrease the likelihood of antibody formation.

weight and increased perinatal wastage with the later development of diabetes.

Gilbert and Dunlop (1949) and Moss and Mulholland (1957) confirmed these observations. During 1950 Wilkerson initiated classic studies of the maternal history of risk factors for abnormal GTT in pregnancy. Study has been extended by O'Sullivan et al. Various risk factors for gestational diabetes are previous large infant, Family history of diabetes, glycosuria, previous perinatal deaths, obesity, abnormal obstetric history, malformation, hydro-amnios, hypertension, positive glucose challange test, hyperglycemia, prematurity, toxemia, monilia, multiparity, over age more than 35 years, hypoglycemia.

Screening Methods of GTT

Mestman and associates conducted 3 hour OGTT with 100 gm glucose. Patients were classified in three groups - (1) those with family history of diabetes, (ii) those with obstetric history of previous large infant, perinatal loss, prematurity of toxemia in previous two or more pregnancies, and (iii) those with no history to suggest diabetes or previous abnormal obstetric events. Upper limits of blood glucose concentrations were laid as fasting 115 mg/dl, 1 hour 195 mg/dl, 2 hour 150 mg/dl and 3 hour 140 mg/dl. Two values above normal required for diagnosis. Following their criteria, they found the overall prevalence of abnormal glucose tolerance as 14 percent. Abnormal

tolerance was most common (24%) in those with an obstetric prediabetes history, but the sensitivity was low.

Macafee and associates screened 1000 patients at 32 weeks of gestation for risk factors and conducted glucose tolerance test in all. Patients were classified in 4 groups - (i) family history of diabetes, (ii) age ≥35 years, (iii) Maternal obesity (90 kg) and (iv) glycosuria. OGTT was done with 50 gm glucose with upper limits of capillary plasma as fasting 100 mg/dl, 1 hour 170 mg/dl, 2 hour 120 mg/dl and 3 hour 100 mg/dl. One abnormal value required for diagnosis.

Specificity rates were very high with all individual factors but were lower when any factor was used separately. Guttorm in Norway performed OGTT during the third trimester of pregnancy in 514 women. Risk factors were (i) potential diabetes (family history of diabetes, 20% overweight or baby less than 2.5 or more than 4.5 kg), (ii) Glycosuria, (iii) Fasting plasma glucose more than 90 mg/dl two times. Tests were done with 1 gm/kg glucose load and capillary serum was used. 2 and 2½ hour values ≥167 mg% and 145 mg% required for diagnosis.

The most extensive evaluation of risk factors for abnormal glucose tolerance in pregnancy was that reported by O'Sullivan and associates. Glucose tolerance tests were performed on 752 pregnant women, risk factors assessed in this study included (i) previous delivery of infant of

4.1 kg or more, (ii) history of two or more pregnancies of perinatal death, malformations, prematurity, excessive weight gain, hypertension or proteinemia (iii) family history of diabetes, (iv) a serum glucose level of 150mg% or more 1 hour after a 50 gm glucose challange.

The concluded that positive challange test was the most sensitive index of risk factors whether the test was carried out alone or in combination with other factors. The sensitivity and specificity of the positive glucose challange were 79% and 87% respectively.

OGTT was performed with 100 gm glucose load, and upper limits of normal values were fasting 105 mg/dl, 1 hour 190 mg/dl, 2 hour 155 mg/dl and 3 hour 145 mg/dl. Two abnormal values are required for diagnosis.

O'Sullivan's criteria is the most commonly used criteria for the diagnosis of gestational diabetes.

The current recommendation for detection of abnormal glucose tolerance during pregnancy were recently developed by the workshop group of American Diabetes Association, American College of Obstetrician and Gynaecologists and National Institute of Health. All patients who are not known diabetics should be evaluated for risk factors, if any of these factors are present screening test is performed i.e. fasting plasma glucose level $\geq$105 mg/dl or 2 hour post prandial plasma glucose level $\geq$120 mg/dl. All patients with positive screening test should undergo 3 hour OGTT.

Management of Gestational Diabetes

Gestational diabetes is defined as "CARBOHYDRATE INTOLERANCE OF VARIABLE SEVERITY WITH ONSET OR FIRST RECOGNITION DURING PREGNANCY". This condition is associated with increased perinatal mortality if undiagnosed and/or untreated, and with increased perinatal morbidity even when diagnosis is made (American Diabetes Association).

Furthermore, women with gestational diabetes are at significantly increased risk for the subsequent development of diabetes when they are not pregnant. Thus the management of gestational diabetes is directed towards prevention of adverse effect of gestational diabetes.

At present mortality due to gestational diabetes has decreased significantly, because of early diagnosis and active management of gestational diabetes.

All the recent studies include only cases of gestational diabetes, identified and treated in some manner, whether by prescription of diet, administration of insulin, testing of fetal well being or merely by categorization as a pregnancy 'at risk' with the maitenance of increased vigilance by the health care team.

But in older studies gestational diabetes was either undiagnosed or untreated. In these studies perinatal mortality was found to be higher. Petit et al(1980) reported that perinatal mortality rates were directly proportional to the 2 hour plasma glucose level, with

values ⩽120 mg/dl associated with PNM rates of 5 per 1000 and values between 160-194 mg/dl associated with rates of 44 per 1000.

O'Sullivan et al (1973) found a relative risk for perinatal mortality of 4.3 among 187 pregnancies complicated by untreated gestational diabetes compared with 259 randomly selected control pregnancies. Although in both the studies post prandial glucose was measured at each clinic visit, but no therapy was provided, as at that time no treatment goals or estimating of risk were available for gestational diabetes.

All the current studies involved some sort of intervention of intensive surveillence and thus do not represent the gestational diabetes in its undiagnosed state.

Among all the perinatal complication of gestational diabetes macrosomia is the most frequent complication.

In the study of Petit et al there was a direct relationship between 2 hour maternal plasma glucose and likelihood of birth of large baby.

In another study by Tellarigo et al (1986) similar relationship was found between 2 hour value of a 100 gm 2 hour glucose tolerance test and neonatal macrosomia.

According to Pedersen's hypothesis, which states that "maternal hyperglycemia is transmitted to the

fetal circulation, because glucose crosses the placenta readily fetal hyperglycemia results, causing stimulation of fetal pancreatic B cells with resulting fetal hyperinsulinemia, because fetal insulin cannot cross the placenta to help restore normal maternal glucose levels, thus this unphysiological degree of hyperinsulinemia persist in the fetal compartment. Fetal hyperinsulinemia have been implicated in most of the adverse outcome observed in infants of diabetic mothers. Thus management of gestational diabetes is aimed at the prevention of fetal hyperinsulinemia and thus mortality and morbidity. However, prevention is not always successful therefore, another aspect of treatment of gestational diabetes is the early detection of potential morbidity and timely intervention to minimise such problem.

American College of Obstetrician and Gynaecologists and American Diabetes Association suggested that fasting plasma glucose should be maintained below 105 mg/dl and 2 hour postprandial values below 120 mg/dl for gestational diabetic pregnancies. American Diabetic Association recommended that fasting and 2 hour postprandial plasma glucose should be measured at least at weekly intervals.

Gestational diabetic mothers can be managed by dietary modifications in most of cases, only 10-15 percent of gestational diabetics require insulin therapy. Oral

Although there are number of different approaches to using insulin, gestational diabetes particularly amenable is most cases to single daily injection regimens. Most individuals with gestational diabetes who require insulin respond to a morning injection of a mixture of intermediate and short acting insulin. Some require a second injection before dinner, and relatively few requires an intermediate insulin does at bed time.

O'Sullivan et al demonstrated a reduction in the likelihood of macrosomia among infants born to mothers who took prophylactic insulin prescribed without regard to maternal glycemic levels, in contrast with the offspring of gestational diabetic mothers randomised to a control group, who did not receive insulin.

Recently, Oded et al (1991) reported that insulin treatment in patients with gestational diabetes mellitus with fasting plasma glucose more than 5,3 m mol/l significantly reduces adverse perinatal outcome.

Some authors such as O'Sullivan et al, Cowland and Lekin et al have advocated insulin treatment of all gestational diabetics to reduce the incidence of macrosomia.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

The present study was carried out with the following aims and objectives :

1. To study the incidence of abnormal glucose tolerance test in pregnant women.
2. To find out the correlation between abnormal GTT and PIH.
3. To study the mode of delivery in cases of abnormal glucose tolerance test and incidence of caesarean section.
4. To study its correlation with intrapartum complications.
5. To study the incidence of perinatal mortality and morbidity in the study group (Abnormal GTT) and control group.

MATERIAL AND METHODS

MATERIAL AND METHODS

This is a comparative study of evaluation of neonatal complications in infants of mothers having abnormal glucose tolerance and mothers having normal glucose tolerance during third trimester of pregnancy.

Study was carried out over antenatal mothers in antenatal period attending the department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi and infants born to these mothers. The study was conducted in 85 patients (Antenatal mothers) in the department of Obstetrics and Gynaecology, M.L.B. Medical College, Hospital, Jhansi during the year 1994-95.

Antenatal mothers were screened on the basis of certain factors present in history and clinical examination i.e. obesity, age, family history of diabetes, previous history of unexplained perinatal death, previous history of infant born with congenital malformations, polyhydroamnios, hypertension, proteinuria and moniliasis.

These mothers underwent detailed medical history and thorough clinical examination including obstetrical examination.

Mothers with established diabetes were excluded from the study.

METHODOLOGY

Mothers were subjected to 100 gm glucose 3 hours glucose tolerance test, at 30±4 weeks gestation, then at weekly interval, upto one week after delivery.

Criteria for abnormal glucose tolerance test (GTT)

On the basis of 3 hour GTT, mothers having abnormal glucose tolerance were grouped into three categories.

I. Gestational Diabetes

On the basis of O'Sullivan criteria gestational diabetes is diagnosed, if two or more values are abnormal.

O'Sullivan Criteria :

Fasting glucose	- 105 mg/dl
At one hour	- 190 mg/dl
At two hour	- 165 mg/dl
At three hour	- 145 mg/dl.

In our study fasting glucose testing was omitted because it was usually seen normal in previous studies.

II. Impaired Gestational Glucose Tolerance

If two hour plasma glucose levels lies between 140 to 164 mg/dl, this category is defined as impaired gestational glucose tolerance (IGGT).

III. Isolated Abnormalities of blood glucose

If any of the plasma glucose values exceeded the O'Sullivan criteria at the appropriate time (IABG).

Those mothers who showed abnormal test were given suitable dietary advice and if necessary were kept on insulin. Plasma glucose values were estimated every week, so as to keep post prandial plasma glucose value below 120 mg/dl.

Newborn

Newborns of these mothers were subjected to htorough clinical examination and investigations :-

- Weight of the baby at the time of birth.
- Gestation of baby.
- Any congenital anomaly, if present.
- Any clinical evidence of respiratory distress syndrome.
- Any clinical evidence of hypocalcemia.
- Hyperbilirubinemia - all the common causes of pathological jaundice were excluded.

Weight of baby

Weight of bewborn was taken by electronic weighing machine by Lectomedrik. It has got accuracy upto 10 gms weight of the baby was plotted against intrauterine growth charts and babies having birth weight more than 90th percentile for gestational age were termed as macrosomic babies.

Gestational age

Gestational age of baby was estimated by using Dubowitz's criteria. Dubowitz has derived a score based on:

a. External characteristics.

b. Neurological characteristics : This score system is convertable into a graph.

Investigations of Newborn

For the purpose of investigations blood samples of newborn was collected by heel prick method. Investigations included :

a. Plasma glucose estimation 2 hour after birth by hemoglukotest strips using Reflolous-S glucometer.

b. Serum bilirubin estimation (if clinical evidence of hyperbilirubinemia present).

Plasma glucose estimation

Plasma glucose levels in mothers and newborns were estimated by Hemoglukotest 20-800 R. Strip using glucometer named Reflolux-S supplied by Boehringer Mannheim.

Principle

Test is based on glucose oxidase/peroxidase reaction. Hemoglukotest strips react specifically to glucose.

Test area consists of two test zones with different sensitivity to glucose. The lower test zone gives (clearly distinguishable) colour in the range 20-120 mg/dl, and upper test zone in the range of 120-800 mg/dl).

Exact values are determined with the help of Reflolux-S glucometer.

Test strips were protected from humidity and direct sunlight.

Reflolux-S

It is the instrument used for plasma glucose measurement.

Principle

The colour intensity of the reacted strip area is measured by reflectance photometry in Reflolux-A. The instrument is equipped with double beam optical system, capable of evaluating both zones of the test area simultaneously.

Technical Specifications

Type	Reflolux-S
Ranges of measurement	10-500 mg/dl
Wave length	950 nm (infra red)
Power supply	6 volt battery
Storage capacity	Maximum 20 blood glucose value.

Test Procedure

- Finger was pricked with disposable needle after cleaning the test area.
- Test area of hemoglukotest strip 20-800 R was covered with one large drop of blood. Timer pressed immediately.
- At the long buzzer at 60 sec. blood is wiped off with clean dry cotton from the test area of haemoglukotest strip 20-800 R.

- At the 80 second, glukostrip was inserted into the Reflolux-S glucometer facing the test area towards the on off button.
- After 120 seconds, the display automatically shows exact plasma glucose values.

Serum bilirubin measurement

Mitr's bilirubin reagent is used for determination of total and direct serum bilirubin.

Procedure

Three test tubes labelled as B-blank, D-direct and T - total taken.

Reagent	For 3 ml Cuvette (m)		
	B	D	T
1. Diazo blank D reagent	2.0	-	-
2. Diazo working reagent	-	2.0	2.0
3. Serum	0.1	0.1	0.1
4. Reagent C	1.0	-	1.0
5. Distilled water	-	1.0	-

Contents of each tube were mixed thoroughly after each addition.

Optical densities of contents of all the three tubes were measured at 540 $\pm$ 15 nm.

Calculation

$$\text{Total Bilirubin} = \frac{\text{O.D. of T} - \text{O.D. of B}}{\text{O.D. of Standard}} \times 5.0 \text{ mg\%}$$

$$\text{Direct bilirubin} = \frac{\text{O.D. OF D} - \text{O.D. of B}}{\text{O.D. of Standard}} \times 5.0 \text{ mg\%}$$

O B S E R V A T I O N S

OBSERVATIONS

The present study was carried out on 30 abnormal OGTT and 55 normal GTT patients in the department of Obstetrics and Gynaecology, M.L.B. Medical College, Hospital, Jhansi during the year, 1994-95.

AGE INCIDENCE IN CASES OF ABNORMAL OGTT

TABLE I : Distribution of cases according to maternal age.

Maternal age groups (years)	No.of cases	Percentage
21 - 25	5	16.67
26 - 30	15	50.00
31 - 35	6	20.00
36 - 40	4	13.33
TOTAL	30	100.00

Table I shows that out of the total 30 cases studied with abnormal glucose tolerance test, 16.67% were from 21-25 years of age, 50% cases from 26-30 years of age, 20% cases from 31-35 years of age and remaining 13.33% cases were from 36-40 years of age.

TABLE II : Oral glucose tolerance test in third trimester of pregnancy.

OGTT Results	No.of cases	Percentage
ABNORMAL OGTT		
Gestational diabetes	12	14.12
IABG	11	12.94
Impaired	7	8.24
NORMAL GTT	55	64.70
TOTAL	85	100.00

Out of total 85 cases studied, 12(14.12%) cases were having gestational diabetes (i.e. two or more values abnormal of 3 hour 100 gm OGTT).

11 (12.94%) cases were having isolated abnormality of blood glucose (i.e. only one value abnormal).

7 (8.24%) cases were having impaired gestational glucose tolerance i.e. 2 hour plasma glucose tolerance value more than 140 mg/dl.

55 (64.70%) cases were having normal GTT, they served as a control.

TABLE III : Risk factors in mothers with abnormal GTT and normal GTT.

Risk factors	Mothers with H/o of BOH with abnormal glucose tolerance						Total No. of mothers with abnormal GTT		Total No. of mothers with BOH with Normal GTT (55)	
	GDM(12)		IABG(11)		Impaired(7)					
	No.	%	No.	%	No.	%	No.	%	No.	%
Age ≥25 years	10	83.30	10	90.09	6	85.71	26	86.66	28	50.90
Maternal obesity	3	25.00	3	27.27	-	-	6	20.00	3	5.45
Maternal hypertension	2	16.66	3	27.27	-	-	5	16.66	3	5.45
Maternal hydroamnios	3	25.00	1	9.09	-	-	4	13.33	5	9.00
H/o perinatal loss	5	41.66	5	45.45	4	57.14	14	46.66	12	21.82
H/o congenital malformed baby	-	-	-	-	-	-	-	-	-	-
H/o large sized baby	4	33.33	5	45.45	1	12.28	10	33.33	8	14.54

Though all the risk factoes were found with increased frequency in mothers with abnormal GTT. Most common factor was maternal age more than 25 years. It was found in 83.33% cases of gestational diabetes mellitus, 909.90% cases of isolated abnormality of blood glucose and 85.75% cases of impaired GTT. But it was found in only 50.90% of cases of normal GTT mothers.

Second most common factor was previous history of perinatal loss. It was found in 41.66% cases of GDM. 45.45% cases of IABG and 57.14% cases of impaired GTT and 46.66% cases of total abnormal GTT. But it was found in only 21.92% cases of normal GTT.

Third common factor was history of large sized baby in previous pregnancies. It was found in 33.33% cases of GDM, 45.45% cases of IABG and 12.28% cases of impaired GTT and 33.33% cases of total abnormal GTT mothers. But in cases of normal GTT it was only 14.54%.

Other risk factors were also found in increased frequency in cases of abnormal blood glucose tolerance mothers.

TABLE IV : Mode of delivery in cases of normal GTT & abnormal GTT mothers and incidence of LSCS in both groups.

Mode of delivery	Abnormal GTT(n=30)		Normal GTT (n=55)	
	No.	%	No.	%
N.V.D.	17	56.67	41	74.54
LSCS	13	43.33	13	23.64
Forcep	-	-	1	1.82
TOTAL	30	100.00	55	100.00

The incidence of LSCS was about 43.33% in abnormal glucose tolerance mothers as compared to 23.64% of normal GTT mothers which is definitely 2 folds of the normal GTT mothers (Table IV).

TABLE V : Neonatal complications in mothers with normal and abnormal GTT.

Neonatal complications	Abnormal Glucose Tolerance Test								Normal glucose tolerance test (55)	
	GDM(12)		IABG(11)		Impaired(7)		Total(30)			
	No.	%	No.	%	No.	%	No.	%	No.	%
Macrosomia	2	16.66	2	18.88	-	-	4	13.33	4	7.27
Macrosomia+Jaundice	1	8.33	-	-	-	-	1	3.33	-	-
Prematurity	-	-	-	-	1	14.28	1	3.33	2	3.64
N. Jaundice	2	16.66	2	18.88	1	14.28	5	16.66	7	12.72
N. Hyperglycemia	1	8.33	-	-	-	-	1	3.33	-	-
RDS in neonates	1	8.33	1	9.09	1	14.28	3	10.00	1	1.80
Congenital malformation	2	16.66	1	9.09	-	-	3	10.00	6	10.90
I.U.D.	-	-	-	-	1	14.28	1	3.33	5	9.09
TOTAL	9	74.98	6	54.54	4	57.12	19	63.31	25	45.42

TABLE VI : Neonatal complications in mothers with normal and abnormal GTT.

Neonatal complications	Abnormal GTT(12) No.	%	Normal GTT(55) No.	%
Macrosomia	2	16.66	4	7.27
Macrosomia+ Jaundice	1	8.33	-	-
N. Jaundice	2	16.66	7	12.72
Prematurity	-	-	2	3.64
N. Hypoglycemia	1	8.33	-	-
RDS	1	8.33	1	1.80
Congenital formation	2 (Expired)	16.66	6 (Expired)	10.90
I.U.D.	-	-	5	9.09
TOTAL	9	74.98	25	45.42

Among all the complications macrosomia, congenital malformation and jaundice were found with increased frequencies in cases of abnormal GTT. The incidence of macrosomia was 16.66% in cases of abnormal GTT as compared to 7.27% cases of normal GTT. Jaundice was found in 16.66% cases of abnormal GTT GTT as compared to 12.72% cases of normal GTT. Congenital malformation were found in 16.66% cases of abnormal blood glucose as compared with 10.90% of control group.

RDS was present in 8.33% cases of abnormal GTT as compared to 1.80% of the control group.

Hypoglycemia was present in 8.33% cases of abnormal GTT mothers neonates but it was not present in cases of control group.

Though all the complications were seemed more in cases of abnormal glucose tolerance mothers.

Overall out of 12 infants of abnormal GTT mothers 9(74.98%) had complications while out of 55 infants of control group only 25(45.42%) had neonatal complications.

TABLE VII : Neonatal complications in mothers with IABG and mothers with normal GTT.

Neonatal complications	IABG (11)		Normal GTT(55)	
	No.	%	No.	%
Macrosomia	2	18.18	4	7.27
Macrosomia+Jaundice	-	-	-	-
Prematurity	-	-	2	3.64
Jaundice	2	18.18	7	12.72
Hypoglycemia	-	-	-	-
RDS	1	9.09	1	1.80
Congenital malformation	1 (Expired)	9.09	6 (Expired)	10.90
I.U.D.	-	-	5	-
TOTAL	6	54.54	25	45.42

Most common complications in infants of the isolated abnormality of blood glucose mothers were macrosomia and jaundice. It was found 18.18% macrosomia and jaundice each in cases of isolated abnormality of blood glucose as compared to 7.27% of neonatal macrosomia, in Normal GTT mothers and 12.72% jaundice in infants of normal glucose tolerance mothers.

Other complications were also frequently found in isolated abnormality of blood glucose cases but congenital malformation were near about equal in study group and control group.

Overall out of 11 patients of IABG mothers - 6(54.54%) cases had neonatal complications, while out of 55 infants of control group, only 25(54.42%) cases had neonatal complications.

TABLE VIII : Neonatal complications in mothers with impaired glucose tolerance mothers and in cases of normal GTT mothers.

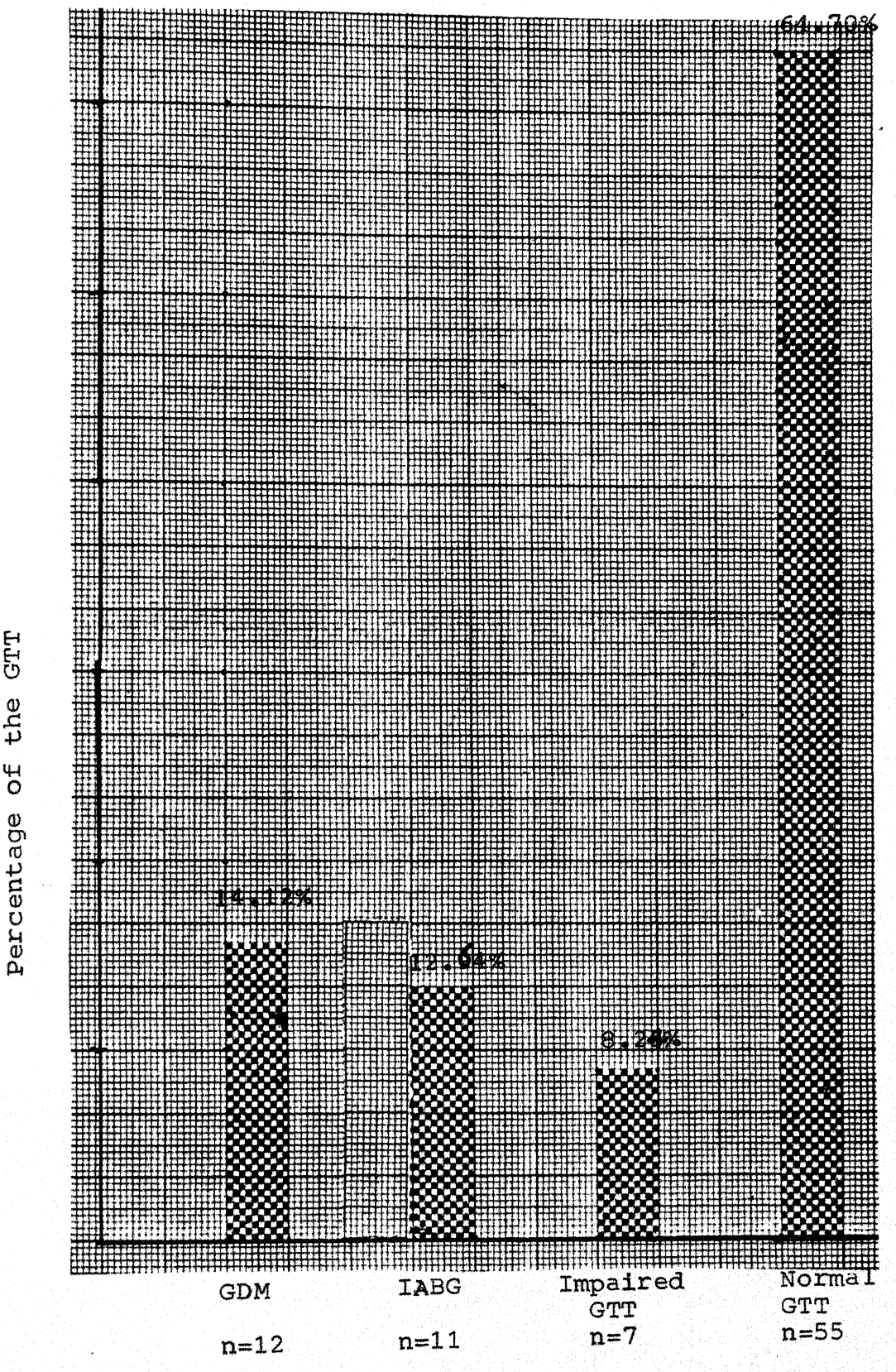
Neonatal complications	Impaired GTT (n=7)		Normal GTT (n=55)	
	No.	%	No.	%
Macrosomia	-	-	4	7.27
Macrosomia + Jaundice	-	-	-	-
Macrosomia + RDS	-	=	-	-
Prematurity	1	14.28	2	3.64
Jaundice	1	14.28	7	12.72
Hypoglycemia	-	-	-	-
R.D.S.	1	14.28	1	1.80
Congenital malformation	-	-	6	10.10
I.U.D.	1	14.28	5	9.09
TOTAL	4	57.12	25	45.42

Though all the complications except macrosomia and congenital malformation were found in increased

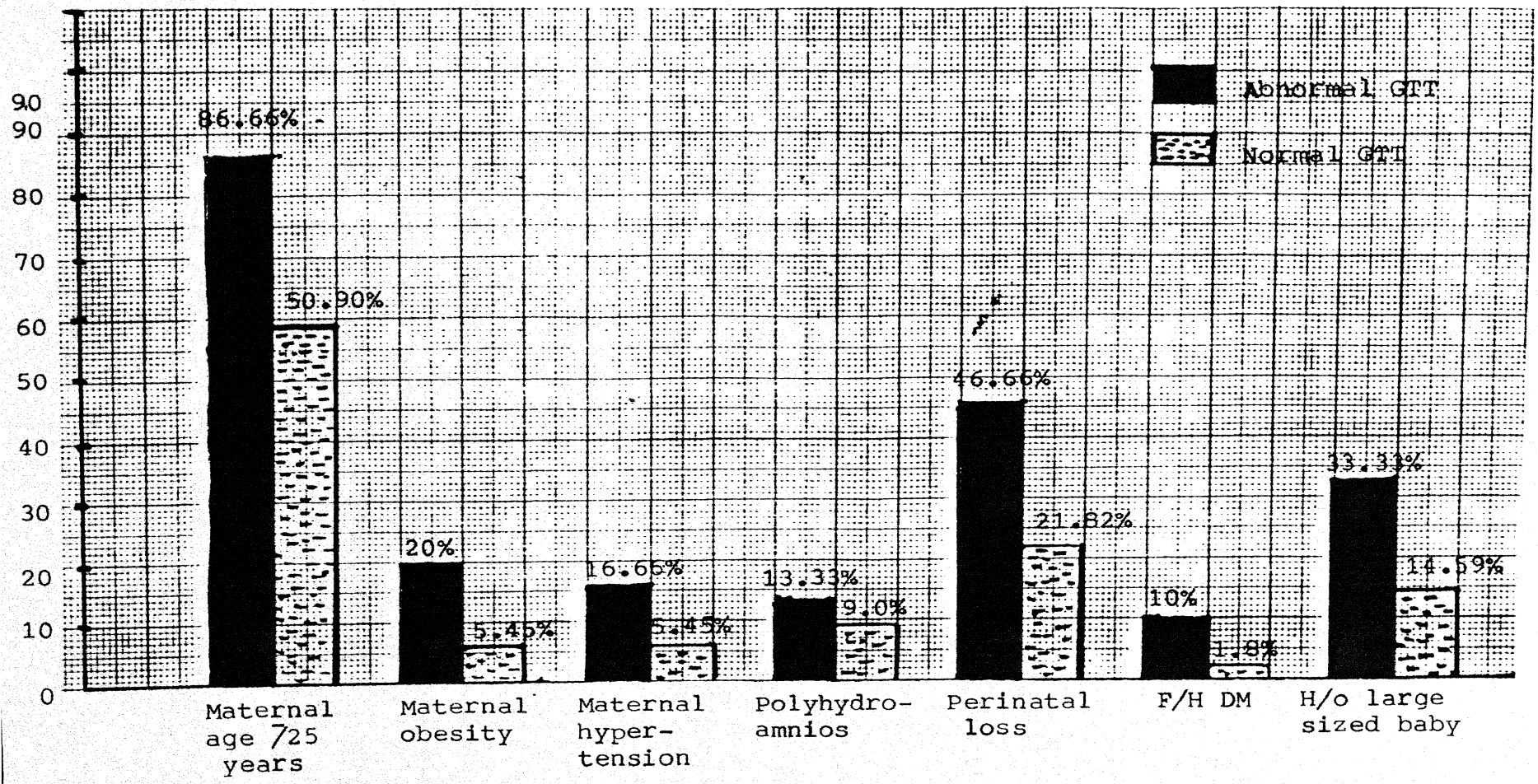
frequency among the impaired glucose tolerance mothers infants. Prematurity was seen in 14.28% infants of impaired glucose tolerance mothers as compared to 3.64% in cases of control group.

RDS was present in 14.28% infants of impaired GTT mothers as compared to only 1.80% infants of control group.

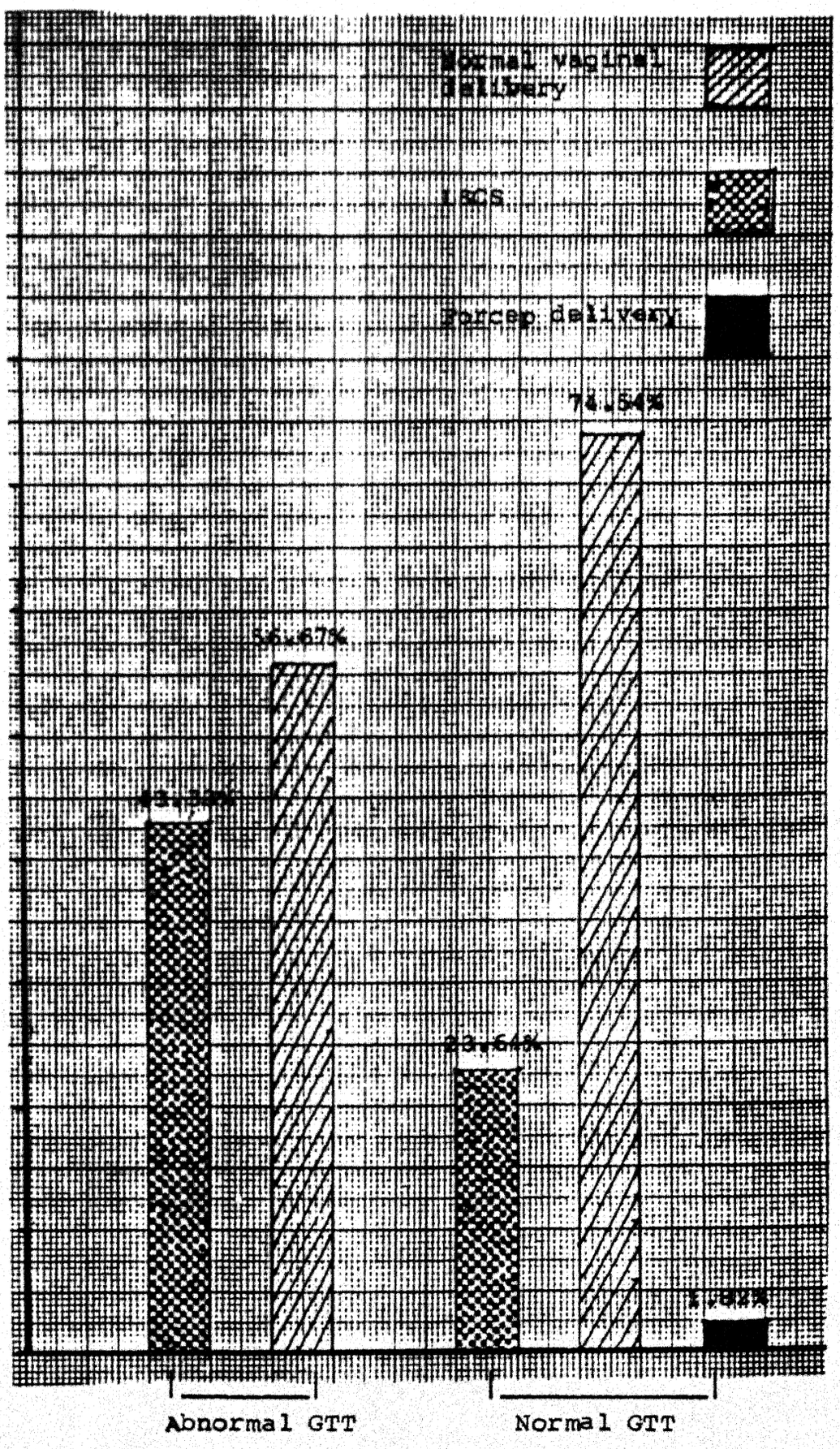
Jaundice was found near about equal in both groups of mothers infants, it was seen in 14.28% of impaired glucose tolerance mothers infants as compared to 12.72% infants of control group.



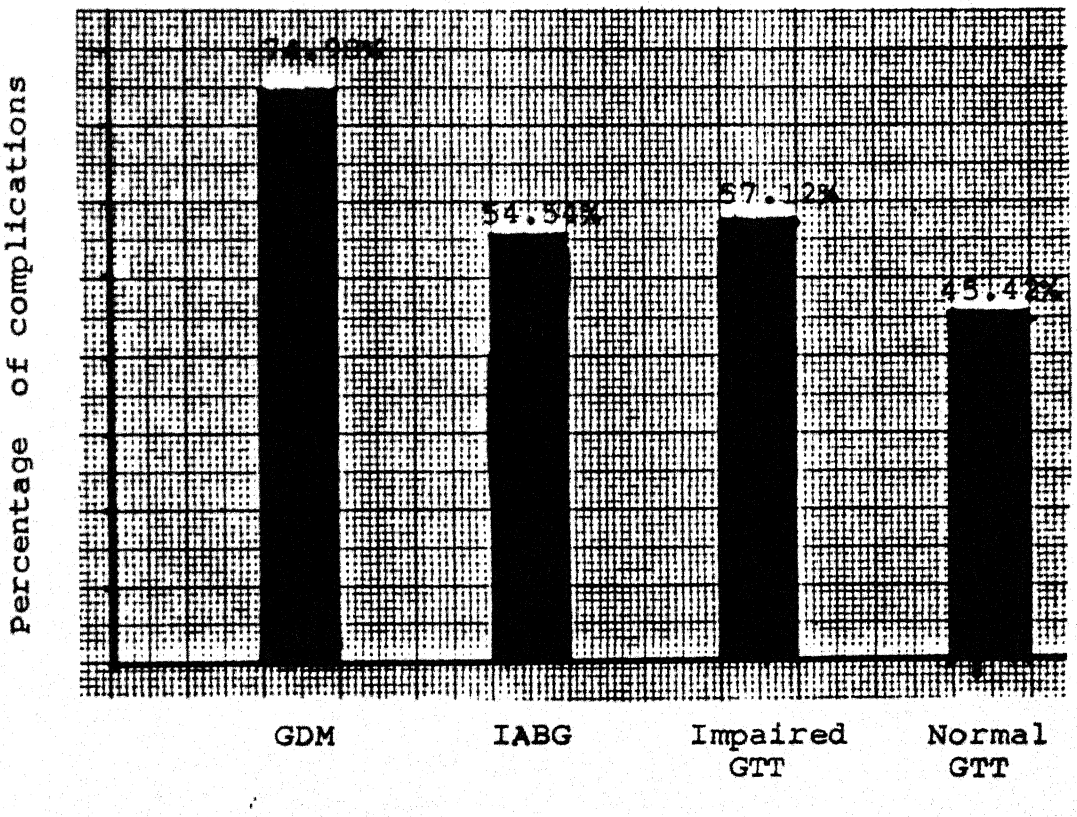
Incidence of abnormal GTT and normal GTT.



Percentage of risk factors in cases of abnormal glucose tolerance mothers and normal glucose tolerance mothers.



The incidence of LSCS in the normal GTT mothers and abnormal glucose tolerance mothers and percentage of the normal vaginal delivery in the study group and control group.



Neonatal complications in mothers with abnormal glucose tolerance and in mothers with normal glucose tolerance. test.

D I S C U S S I O N

DISCUSSION

Many metabolic and hormonal changes occur in the body during pregnancy. These are physiological changes in response to pregnant state, changes in the maternal carbohydrates metabolism is one of them. The overall effects of these alterations in maternal carbohydrate metabolism in normal non diabetic women are reduced fasting blood sugar and amino acid levels. But increased post prandial blood sugar, free fatty acids, ketone, triglycerides and insulin secretions in response to glucose (Phelps et al). Though the insulin secretion is increased, but simultaneously body develop resistance to insulin because during pregnancy, there is increased production of insulin antagonising hormones like hPL, Oestrogen progesterone and cortisol women who are not able to increase the pancreatic insulin secretions sufficiently to overcome pregnancy induced insulin resistance, develops gestational glucose intolerance.

Maternal hyperglycemia leads to various maternal and neonatal complications. Present study gives information about association of risk factors in mothers having abnormal glucose tolerance and various neonatal complications in infant born to such mothers.

Overall incidence of gestational diabetes is approximately 2% (O'Sullivan et al, 1964).

Stephen et al (1981) studied incidence of gestational diabetes between 1-5%.(Gabbe (1985) studied that the incidence of GDM has been between 3-15% depending upon the population studied and diagnostic criteria used. In the Malaysian hospital Nik (1988) found 1-3% incidence. Deodari et al in their study reported the incidence of gestational diabetes as 55/11,920 while Tellorigo and associates (1987) reported the incidence of impaired gestational glucose tolerance 16%. In our study we found the incidence of gestational diabetes 14.12% and of IABG 12.64% and impaired 8.24%. In our study incidence of the GDM is higher than the O'Sullivan study but coming in the range of study of Gabbe (1985). While the incidence of the impaired glucose tolerance test is lesser than the observation observed by Tellarigo.

Increasing maternal obesity, age and family history of diabetes are associated important risk factors for GDM. [O'Sullivan et al (1973), Maresh and Beard (1989) and Roseman et al (1991)]

Mestman (1980) reported that the incidence of GDM was 3.7% in women younger than the 20 years of age, 7.3% for those 20-30 years of age, 3.8% for women older than the 30 years of age.

In our study we found 16.66% cases ⩽25 years of age, 50% cases between 26-30 years of age and 20% of the cases between 31-35 years of age and 13.33% cases more than 35 years of age. Which in quite higher than the previous study.

Analysis of risk factors in mothers with abnormal glucose tolerance test

In our study we found most common risk factor age 725 years, which was also seen by the O'Sullivan et al (1973), Maresh and Beard (1989) and Roseman et al (1991).

Second most common factor was history of previous perinatal loss, it was found in 46.66% of the abnormal glucose tolerance mothers as compared to 21.82% of the normal GTT.

Third most common factor was previous history of large size of baby which was found in 33.33% of the GDM, 45.45% of cases of IABG and 33.33% cases of the impaired glucose tolerance test.

Oat et al (1980) reviewed the results of a 50 gm 3 hours OGTT performed in 137 who delivered an infants weighing more than 4540 gm. Only 32(23%) had an abnormal GTT which is similar to the our study.

In our study we found polyhydro-amnios in 25% cases of the GDM and 9.09% cases of the IABG. Which is near about equal to the previous study i.e. 20% by Joslin diabetes mellitus.

In our study hypertension was found in 16.66% cases of GDM and 27.27% of the isolated abnormality of the blood glucose which is similar to the studied in the teritiqrry Malaysian hospital KualaLumpur - 10.20%.

Robert et al studied that normal delivery occurred insignificantly fewer of the patients with impaired glucose

tolerance 63.3% than in those with normal glucose tolerance 74.3% and in only 34.8% of those with type I diabetes mellitus. There were no differences in the rates of instrumental delivery but there were significantly greater caesarean section rates in those with abnormal GTT mothers.

In our study we found 43.39% incidence of LSCS in cases of the abnormal glucose tolerance mothers as compared to the 23.64% in normal glucose tolerance mothers and the incidence of the normal vaginal delivery is 56.67% in abnormal glucose tolerance mothers as compared to 74.54% in cases of the normal glucose tolerance mothers. Our study shows the incidence of normal vaginal delivery were about to the previous study and shows the greater incidence of caesarean section.

The major finding of this prospective study of infant born to mothers with abnormal GTT is macrosomia, congenital malformations and jaundice which were found in increased frequency in cases of abnormal GTT. Macrosomia was found in 16.66% cases of the GDM, 18.18% cases of IABG. In earlier study Deodari and coworkers reported 34.5%, E. Stenninger reported 29% incidence of macrosomia in insulin treated GDM. While Tellarigo reported the macrosomia in 27.5% of infants born to mothers with GIGT. According to Philipson et al (1985), Gabbe et al (1979) and Coustan and Lewis (1978) fetal macrosomia upto 30% infants of mothers with abnormal GTT. In his study Moshe Hod et al reported the incidence of macrosomia 5.6-20% in diabetic mothers.

The finding of our study is near about equal to the previous study.

Another important findings of our study was congenital malformation we found 2 infants (16.66%) cases out of 12 cases of GDM and one infants (9.09%) out of the 11 cases of the IABG, had major congenital anomaly. No infant was found with minor congenital anomaly. Thus total 3 infants out of 30 abnormal GTT mothers had congenital anomaly, 2 of them had anencephaly and one had hydrocephalus. Normal GTT mothers also gave birth to the congenital malformed baby. But it was found in only 10.9% mothers who had normal GTT. Thus from above observation it seems that the incidence of congenital malformation was more in cases of abnormal glucose tolerance mothers.

In previous study, Moshe Hod et al reported the incidence of minor anomaly between 19.4-20.5% and major congenital anomalies 1.8-6.82%. Joslin diabetes observed incidence of the congenital anomalies 9% major and 5% minor.

Our observations is near to the observations observed by Joslin Clinic. The cause of the congenital malformation is probably related to alteration in metabolic milieu in early pregnancy.

Increased incidence of the neonatal hyperbilirubinemia is another frequent complications of diabetic pregnancies. The cause of it is presumed to be related to functional prematurity of the hepatic enzymes (Osler and co-workers). In our study we found 16.66% neonatal jaundice in cases of GDM and 18.18% in cases of IABG and 14.28% cases

of the impaired GTT. While neonatal jaundice was present only in 12.72% cases of the normal GTT mothers.

In previous studies Pedersen reported 38.9% incidence of hyperbilirubinemia and in 27% cases studied by Essex and co-workers. Thus the observation of the our study is near about to the previous studies. Moshe et al reported the prevalence of the hyperbilirubinemia as 8.2 - 15.1%.

Another important cause of the neonatal mortality and morbidity in infants born to mothers with abnormal GTT is RDS. Epstein and co-workers concluded that maternal hyperglycemia leads to fetal hyperglycemia resulting in fetal hyperinsulinemia and this results in reduction in ability to fetal lungs to synthesize, store and release lecithin (the primary pulmonary component of surface active material in lungs).

AY Ranade and associates in their study reported 7% infants with RDS in cases of GDM mothers. Similar observation was done by Robert and associates. Our observation is nearly similar to the previous observations as we found RDS in 8.33% cases of GDM mothers and 9.09% cases of IABG mothers and 14.28% cases of impaired GTT mothers. While RDS was present in only 1.8% cases of the normal GTT mothers.

Prematurity was reported in 5% IGDM by Ranade et al. While Deodari et al reported prematurity in 20% infants of GDM. Bur in our study we did not find any prematurity in

cases of GDM mothers and IABG mothers. But it was 14.28% in cases of impaired GTT mothers. Various factors as maternal hydro-amnios, placental insufficiency are incorporated in the eliciting of prematurity.

A common problem in infant born to mothers with abnormal GTT is early post natal hypoglycemia, secondary to excessive insulin secretion after division of umbilical cord and termination of placental transfer of glucose. Hypoglycemia occurs most frequently 2 hours after birth (E. Stenninger et al).

In our study we found hypoglycemia in 83.3% cases of the GDM mothers but none of the cases seen in IABG and impaired GTT mothers. It was also not found in cases of normal GTT. Similar observations was done by Ranade et al. Deodary indicated that risk of neonatal hypoglycemia increased with increasing maternal blood glucose at delivery (Kuhl et al). Thus good control of the maternal hyperglycemia at term can reduce the risk of the neonatal hypoglycemia.

Prevalence of polycythemia was reported 3.8-13.8% in IGDM by Moshe etal. Similar observations were done by Ranade et al and Deodari. Prevalence of polycythemia in normal neonatal population in 1-2%. But in our study we did not found any cases of the polycythemia in either study or control group. According to Pedersen hypothesis maternal hyperglycemia leads to foetal hyperinsulinemia which in turn

suppress the synthesis, storage and release of surfactant leading to HMD. These pulmonary complications of the diabetes leads to fetal hypoxemia than foetal hypoxemia stimulate the haemopoitic sytem leading to polycythemia.

Following early detection and management of GDM fetal morbidity and mortality are increased.

O'Sullivan et al (1973) studied all pregnant women from 1962-1970 4(1.5%) out of 295 women with normal GTT had perinatal loss as compared to 12(6.4%) of 187 were with abnormal GTT.

Hadden (1975) reported 7-9.8% incidence of perinatal mortality in cases of the abnormal GTT.

Abell and Beischer (1995) reported that abnormal GTT was associated with perinatal mortality 31.7/1000 as compared with 9.8/1000 if glucose tolerance was negative. Gabbe et al (1977) showed that perinatal mortality was 19/1000 in IGDM. Deodari et al reported perinatal mortality as 3.5% in IGDM. In our study the incidence of perinatal mortality was 20% while in normal GTT mother it was 12%. Congenital malformation in the form of anencephaly and hydrocephaly.

Pedersen who showed that 20% of perinatal mortality in IGDM is due to the major congenital malformation. One infant died due to RDS and which is another cause of the perinatal mortality as described (Discoll et al).

The main goal is the management of diabetic pregnancy to achieve adequate metabolic control. American College of Obstetric and Gynaecology and Diabetic Association of America, showed the fasting plasma glucose should be maintained below 105 mg% and 2 hour postprandial value ⟨120 mg% for gestational diabetic mothers. GDM can be managed by the dietary modification in only 10-15% of the patients required insulin therapy.

In our study all of the cases were treated with dietary control and only 2 patients required insulin.

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

Maternal hyperglycemia is associated with increased perinatal mortality if undiagnosed and/or untreated and with increased perinatal morbidity even when diagnosis is made. Furthermore, women with gestational diabetes are at significantly increased risk for the subsequent development of diabetes when they are not pregnant. Gestational diabetes is associated with increased maternal complication also, which are UTI, hydroamnios, pre-eclampsia, still birth etc.

The present study gives information about incidence of abnormal GTT during pregnancy, post partum and its correlation with pregnancy outcome. It also gives information about association of the maternal risk factor with abnormal glucose tolerance mothers and neonatal complications in these mothers.

Study was carried out over 85 antenatal mothers with following any one of the risk factors :

1. Obesity.
2. Family history of diabetes mellitus.
3. Previous history of unexplained perinatal death.
4. Previous history of infant born with congenital malformation.
5. Maternal polyhydroamnios.
6. Maternal hypertension.
7. Previous history of over weight baby.

These antenatal mothers were subjected to 3 hour 100 gm OGTT. On the basis of results of OGTT these women were categorised into two groups :

1. Mothers with normal GTT.
2. Mothers with abnormal GTT.

Abnormal GTT mothers were further classified into three groups :

I. Gestational diabetes mellitus.

II. Isolated abnormality of blood glucose.

III. Impaired glucose tolerance.

Out of total 85 patients, 12 had gestational diabetes mellitus, 11 had isolated abnormality of blood glucose and 7 had impaired glucose tolerance while 55 mothers had normal GTT and these 55 mothers were served as a control group.

Mothers with abnormal GTT were subjected to 3 hour OGTT at weekly interval till termination of pregnancy and one week after delivery.

The major risk factors found with higher frequency in mothers with abnormal glucose tolerance test were age more than 25 years, previous perinatal loss and previous history of large sized baby. Most of the patients with abnormal GTT were managed with dietary control. Only two patients required insulin.

There were increased incidence of caesarean section in cases of the abnormal GTT mothers as compared to the normal GTT mothers.

Neonatal complications were also found with higher frequency in the mothers with abnormal glucose tolerance as compared to the normal mothers. Incidence of macrosomia was 16.66% in GDM, 18.18% in IABG as compared to 7.27% in normal glucose tolerance mothers. Incidence of neonatal jaundice was 16.66% in GDM, 18.18% in IABG, 14.28% in impaired glucose tolerance test as compared to 12.72% in normal glucose tolerance mothers. Congenital malformation was 16.66% in GDM, 9.09% in IABG as compared to 10.90% in the normal GTT mothers. RDS 8.33% in GDM, 9.09% in IABG, 14.20% in impaired GTT mothers as compared to 1.80% in normal glucose tolerance test mothers another neonatal complications were also found with abnormal glucose tolerance test is increased frequency.

The following conclusions were drawn from the present study.

1. Incidence of various abnormal glucose tolerance test in Bundelkhand region are as follows :

   GDM - 14.12%

   IABG - 12.64%.

2. Increased incidence of the caesarean section in cases of the abnormal glucose tolerance 43.33% as compared to 23.64% in cases of normal glucose tolerance mothers.
3. There is increased percentage of the maternal complication in cases of the abnormal GTT as compared to the normal GTT mothers.

- Maternal age ≥25 years was found in 86.68% cases of the abnormal GTT as compared to the 50.90% cases of the normal GTT mothers.
- Previous history of perinatal loss 46.66% cases were found in cases of abnormal GTT as compared to the 21.82% cases of the normal GTT.
- Maternal hypertension was found in 16.66% cases of the abnormal GTT mothers as compared to 5.45% cases of the normal GTT mothers.
- Previous history of overweight baby was found in 33.33% cases of the abnormal GTT as compared to the 14.54% cases of the normal GTT.
- Family history of DM was found in 10% cases of the abnormal GTT as compared to the 1.82% cases of the normal GTT

4. Neonatal complications including perinatal mortality are higher among infants born to abnormal GTT mothers as compared to normal GTT mothers. Macrosomia was present in 16.66% cases of the GDM, 18.18 cases of the IABG as compared to the 7.27% cases of normal GTT mothers. Neonatal jaundice was found in 16.66 cases of the GDM, 18.18% cases of the IABG, 14.28% cases of the impaired GTT mothers.as compared to 12.72% cases in normal GTT mothers. Congenital malformation was 16.66% in GDM, 9.09% in IABG as compared to 10.90% in normal GTT

mothers. RDS was 8.33% in GDM, 9.09% in IABG, 14.20% in impaired GTT mothers as compared to 1.80% in normal GTT mothers. Neonatal hypoglycemia was found in cases of the GDM 8.33%. None of the infants in normal GTT were hypoglycemic.

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